# Managing mechanical ventilation: Clinical challenges 2024

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**ABSTRACT**

*Positive pressure mechanical ventilation (PMV) has provided effective life support to millions of patients over the past century. PMV safety, however, has been an ongoing clinical challenge over this same time period. In this article, four "hot topics" with regard to PMV safety are discussed: ventilator-induced lung injury, air trapping, patient-ventilator asynchronies, and self-inflicted lung injury. Evidence-based approaches to recognition and management of these issues are presented and supplemented by novel thoughts from recent literature.*

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Positive pressure mechanical ventilation (PMV) is a life-support technology that has been used extensively around the world for almost a century. PMV has proven to be very effective at supporting gas exchange (oxygenation and $CO_2$ removal) yearly in millions of patients with a variety of cardiorespiratory disorders. However, PMV safety related to potential patient harm from PMV has been the subject of growing concern, especially over the past 3 decades, and a number of issues have been identified.

Chief among these safety concerns is ventilator-induced lung injury (VILI) from excessive stress and strain on alveolar structures.[1–4] To address this, evidence-based guidelines have been developed over the past 3 decades that focus on "lung protective" ventilator settings.[5,6] These focus heavily on limiting maximal and tidal lung "stretch" and reducing repetitive alveolar opening-closing phenomenon. An important clinical question today, however, is whether simply following these guidelines[5,6] is enough?

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There are other important considerations in providing safe PMV. Current "hot topics" include the recognition and management of air trapping,[7] the recognition and management of patient-ventilator asynchronies during assisted ventilation,[8,9] and the recognition and management of the newly appreciated potential for "self-inflicted" lung injury (SILI) from excessive patient inspiratory efforts.[10,11] Clear evidence-based guidelines that address these challenges do not exist today.

The remainder of this article attempts to provide insights into these issues. Note that this is not a comprehensive systematic literature review on mechanical ventilation management. Rather, it is a selective commentary on issues that commonly face clinicians at the bedside based on relevant literature and many decades of experience. It is hoped that these discussions will aid in providing safer approaches to providing PMV in the future.

## Is Following Current Evidence-Based Guidelines Enough to Provide Optimal Effective and Safe PMV?

In 2000, the National Institutes of Health Acute Respiratory Distress Syndrome Network published the seminal study that shows important outcome benefits in patients receiving PMV by using strategies that limit pressures and volumes.[12] Subsequent confirmatory studies have led to guidelines based on the following principles[5]: (1) limit maximal end-inspiratory transpulmonary pressure (often estimated by the airway plateau pressure [Pplat]) to <25–30 cm $H_2O$, (2) limit tidal volume ($V_T$) to <8 mL/kg ideal body weight (IBW), and (3) provide positive end expiratory pressure (PEEP)/inspired fraction of oxygen ($FiO_2$) combinations by using tables that balance partial pressure of arterial oxygen ($Pa_{O_2}$) (55–80 mm Hg), Pplat (<30 cm $H_2O$), and $FiO_2$ < 0.60 targets.

In the past 2 decades, evidence that supports two additional strategies that build on these principles have been reported. One uses assessments of respiratory system compliance during $V_T$ delivery (stress index [SI] and

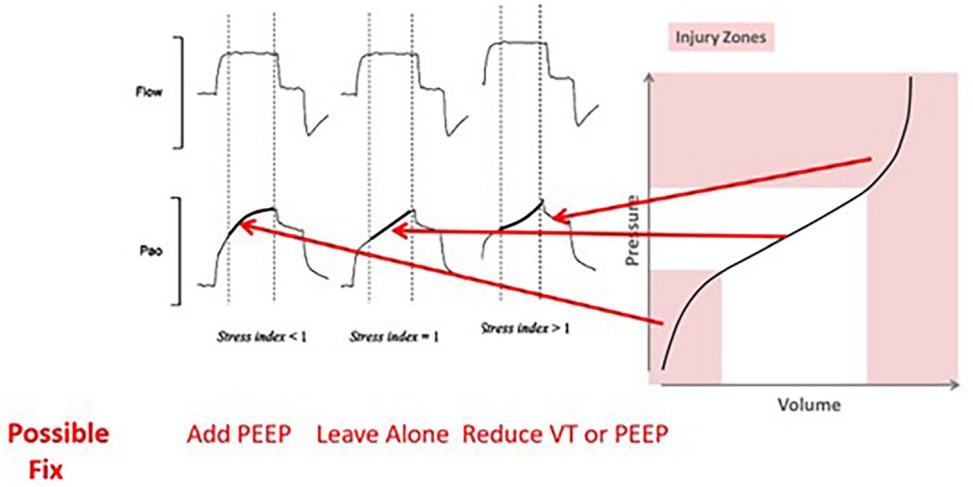


***Figure 1.*** *The stress index as a reflection of respiratory system compliance during tidal breath delivery. The airway pressure over time pattern is assessed during a controlled mechanical breath with a constant inspiratory flow. If compliance is improving during breath delivery (left panel: the pressure profile bends downward), then it suggests recruitment is occurring during inspiration (and thus de-recruitment is occurring during expiration). A possible "fix" is to add PEEP. If compliance is stable during breath delivery (center panel: the pressure rise is steady), it suggests that compliance is unchanging during breath delivery and no adjustments are needed. If compliance is worsening during breath delivery (right panel: the pressure profile bends upward), it suggests that overdistention is occurring during inspiration. Possible "fixes" include tidal volume reduction or PEEP adjustment. PEEP = Positive End Expiratory Pressure (adapted from Ref. 13).*

driving pressure [DP]). The second goes beyond using static volume and pressure measurements, and incorporates time into the calculation of mechanical power to more comprehensively describe the mechanical forces involved in VILI.

*Respiratory System Compliance during Tidal Breath Delivery.* Static pressure-volume (PV) relationships of the whole respiratory system have been used for decades to calculate total system compliance, upper and lower inflection points, and hysteresis. The static respiratory system PV maneuver, however, is technically challenging and attempts to use this assessment to guide PMV settings have not yielded strategies consistently linked to important clinical outcomes.

A more focused approach is to assess PV relationships only during $V_T$ delivery.[2,13–17] This would usually be done after guideline-based settings described above have already been applied. In a sense, this results in a "fine tuning" strategy rather than an initial guide to PMV settings.

The simplest approach is to measure the distending pressure required for tidal breath delivery (Pplat-PEEP). Termed the "driving pressure (DP)," it is driven by respiratory system compliance at end-expiration (CRS) and delivered $V_T$ (*i.e.,* DP = $V_T$/CRS). Indirect evidence from retrospective analyses of large trials of PEEP management and clinical outcomes suggests that a DP > 13–19 cm $H_2O$ is associated with a worse mortality. This would suggest that a DP fine tuning strategy of adjusting $V_T$ and/or PEEP (within current guideline ranges) to achieve lower DPs is a rational addition to Acute Respiratory Distress Syndrome (ARDS) management guidelines.[5,6]

A more sophisticated use of compliance measurements during $V_T$ delivery is to actually measure changes in compliance during breath delivery (Fig. 1). A pattern of improving compliance suggests that recruiting is occurring during inspiration (and by extension, de-recruitment is occurring during expiration). In contrast, a pattern of worsening compliance during breath delivery suggests that overdistention is occurring. These patterns can guide setting adjustments: increasing PEEP to increase recruitment; decreasing $V_T$ and/or PEEP to decrease overdistention.

A practical way to assess compliance changes during breath delivery is to calculate a "stress index (SI)." This requires a passive patient on controlled mechanical ventilation receiving a constant inspiratory flow. The purpose of a constant inspiratory flow is to minimize changes in airway pressure from flow-resistive characteristics. The exponent in the mathematical representation of the PV relationship is the SI. An SI value near one suggests a straight diagonal pressure profile that indicates no recruitment or overdistention is occurring. A value of <1 suggests recruitment is occurring; a value of >1 suggests overdistention is occurring. Fine tuning PMV settings by using the SI is conceptually appealing but meaningful outcome evidence that supports this approach is lacking.

A second fine-tuning strategy involves calculating the ventilator's power of breathing.[18,19] Current evidence-

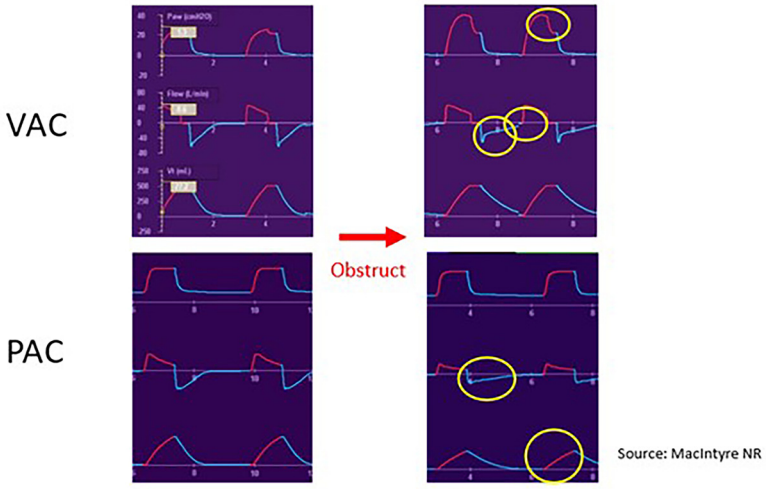


***Figure 2.*** *Airway obstruction, producing air trapping affects volume-assist control (VAC) differently than pressure-assist control (PAC). Pictured are airway pressure, flow, and volume over time before and after an airway obstruction. In VAC, peak-plateau airway pressure increases, expiratory flow is diminished and/or prolonged, and expiratory flow does not reach zero before the next breath is delivered (circles). In PAC, expiratory flow is also diminished and/or prolonged, but pressures do not change and volume is reduced (circles).*

based guidelines focus on minimizing airway pressures and delivered volumes. These are two static measurements that describe the force applied on the lung during a tidal breath and when multiplied together can be expressed as the work per breath (W = mean P × V).

Mechanical power incorporates the element of time (*i.e.*, power = work/time). Intuitively, this should enhance the capabilities of pressure and volume to predict VILI outcomes. Results of small clinical studies[18,19] suggest that this may be true, but to our knowledge large outcome-based studies that compare work versus power-based prediction models do not exist.

In practice, a strategy to minimize power while keeping work/breath constant would be to reduce the respiratory rate. It is important to point out that, if the patient simply replaces machine breaths with spontaneous breaths, then there may be minimal effects to lowering the set rate. A reduction in minute ventilation (MV) from a lower rate will produce hypercapnia. The most important adverse consequences of hypercapnia are hemodynamic (dysrhythmias and hypotension), Modest levels of hypercapnia are often well tolerated and, at least in theory, may be a reasonable trade-off to reduce VILI risk.

### Identifying and Managing Air Trapping

Air trapping describes the phenomenon of end-expiratory lung volumes being above the normal functional residual capacity or relaxation volume.[7,20] Air trapping is sometimes labeled hyperinflation or breath stacking, which reflects the inability of the lung to completely empty and return to an end-expiratory transpulmonary pressure near zero (Fig. 2). Air trapping is driven by factors that impair expiratory flow (airway narrowing, reduced elastic recoil), high MV, and short expiratory times (long Inspiratory (I): Expiratory (E) ratios). High end-expiratory lung volumes and transpulmonary pressures increase the potential for overdistention lung injury, increase dead space ventilation, impair assisted breath triggering, and can compromise cardiac filling.

Air trapping during PMV should always be suspected in patients with obstructive airway diseases (OAD) and high MV requirements.[20–22] In volume-targeted modes of ventilation, air trapping will increase end-inspiratory Pplats; in pressure-targeted modes of ventilation, air trapping will reduce the $V_T$. The classic sign of air trapping on a ventilator is the expiratory flow signal not returning to zero before the onset of the next breath. Under these conditions, an expiratory pause (*i.e.*, expiratory circuit occluded) at end-exhalation will allow trapped gas pressure to equilibrate with circuit pressure and quantify the trapped pressure or intrinsic PEEP (PEEPi). It is important to note that, in severe airway disease, actual airway collapse can terminate expiratory flow before complete lung emptying and thus these classic air-trapping signs may not be evident. Radiologic hyperinflation, assisted breath triggering difficulties, high dead-space ventilation, and cardiac compromise should alert the clinician to the likelihood of air trapping, even when monitored expiratory flow reaches zero at end-exhalation.

Air trapping during PMV should be minimized as much as possible for all of the reasons noted above. This involves minimizing MV as much as possible (including toleration of $CO_2$ elevation: "permissive" hypercapnia), lengthening expiratory time as much as possible, and optimizing bronchodilator therapy. Minimizing MV requirements through appropriate sedation (or even neuromuscular blockade), and fever control can help. A respiratory acidosis (pH values as low as 7.0) may be a viable trade-off to reduce air trapping if cardiovascular function is acceptable. A dramatic scenario is the development of air trapping to such an extent that cardiovascular collapse is

imminent. Under these conditions, temporary separation of the patient from the ventilator can be life saving.

Atelectasis is not a common feature in OAD with air trapping, and thus PEEP to prevent de-recruitment is rarely needed. However, PEEP application can still help in two other ways. First, in a minority of patients with OAD and with severe air trapping, PEEP application below the PEEPi may "splint open" collapsed small airways to allow some lung emptying.[23] This is often a trial-and-error exercise in which small amounts of PEEP are applied and the Pplat response is observed. A reduction in Pplat suggests air trapping has been reduced.

A second PEEP effect in OAD may be to reduce an inspiratory threshold load for assisted breath triggering.[24] This phenomenon is driven by the fact that end-expiratory lung volumes and pressures may be 5–20 cm $H_2O$ above ventilator circuit pressures and this pressure gradient must be overcome by the patient before ventilator circuit pressures can fall to a level that triggers a breath. Clinically, this appears as an obvious patient effort but with delayed or absent ventilator response. Adding small amounts of applied PEEP below the PEEPi level can narrow this gradient and improve triggering. (Fig. 3). This is usually a trial-and-error process: titrate applied PEEP slowly (usually <10 cm $H_2O$) and, if successful, the clinician will observe less triggering delay and more consistent ventilator triggering responses.

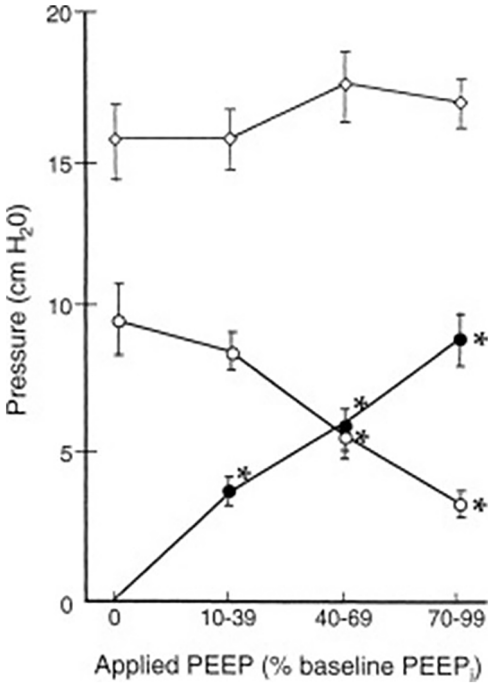


***Figure 3.*** *Lung pressure effects of adding PEEP in the setting of an inspiratory threshold load induced by air trapping (intrinsic PEEP or PEEPi). Pictured are end expiratory esophageal pressure (open diamonds), patient effort to trigger an assisted breath (open circles), and airway PEEP (closed circles) as PEEP is applied as a percentage of measured PEEPi). Note that patient effort is progressively reduced when PEEP is added but end-expiratory esophageal pressure changes little. In this patient, the lowest inspiratory pressure load on the patient is when airway PEEP is just below measured intrinsic PEEP (75–90%) PEEP = Positive End Expiratory Pressure; PEEPi = intrinsic positive end expiratory pressure (reproduced from Ref. 24).*

**Patient Ventilator Interactions: Synchrony and Asynchrony**

Mechanical ventilation modes that permit spontaneous ventilatory activity are termed "interactive" modes because patients can affect various aspects of the mechanical ventilator's functions. These interactions can range from simple triggering of mechanical breaths to more complex processes that affect delivered flow patterns and breath timing.[8,9,25,26] Interactive modes allow for muscle "exercise," which, when performed at nonfatiguing or physiologic levels, may prevent ventilator-induced diaphragmatic dysfunction and facilitate fatigue recovery. In addition, permitting spontaneous patient ventilatory activity and using comfortable interactive modes may reduce the need for the sedation and/or neuromuscular blockers that may otherwise be required to prevent patients from "fighting" PMV. Interactions occur during all three phases of breath delivery: breath triggering, flow delivery, and breath cycling (Fig. 4).[27]

*Ventilator Breath Triggering.* Interactive mechanical ventilators must sense a spontaneous effort by either an airway pressure drop or circuit flow change to trigger a mechanical response. Even with modern sensors, however, there is unavoidable asynchrony in the triggering process. First, a certain level of insensitivity must be incorporated in the sensor to avoid artifacts triggering the ventilator (*i.e.*, "autotriggering"). Second, even when the patient effort has been sensed, valving systems have a certain inherent delay (up to 100 msec or more) before they physically open and achieve target flow into the airway (system responsiveness). Both of these factors can result in uncomfortable "isometric-like" pressure loads on the inspiratory muscles during the triggering process. It is incumbent on the clinician to optimize trigger sensitivity and responsiveness.

As noted above, in the setting of air trapping and PEEPi, the elevated alveolar pressure at end-expiration can serve as a triggering threshold load on the inspiratory muscles. Under these conditions, judicious use of applied PEEP can equilibrate expiratory pressure throughout the lungs and ventilator circuit to reduce this triggering load.

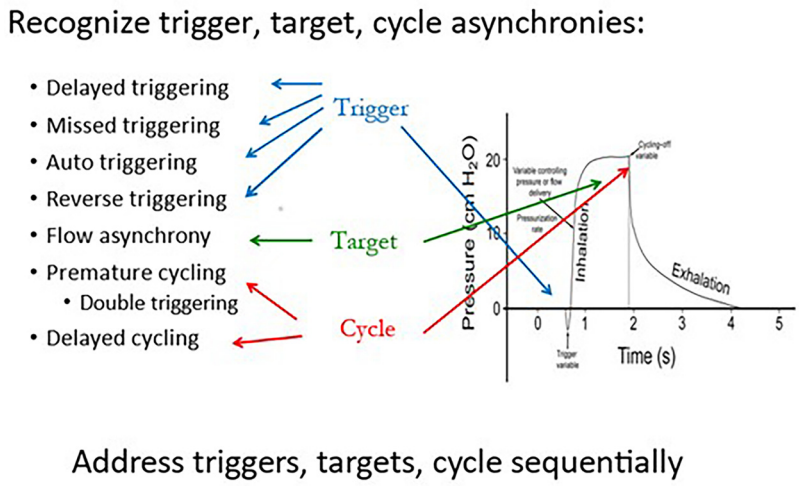


***Figure 4.*** *Patient-ventilator asynchronies can affect all three phases of breath delivery: triggering, flow delivery, cycling. Pictured is the airway pressure profile over time of a patient's interactive breath with locations of various asynchronies. Management involves addressing each breath phase sequentially.*

Excessive triggering can also occur. This may be a consequence of autotriggering from overly sensitive trigger sensors that respond to circuit motion and cardiac oscillations. Extra triggers can also occur if the mechanical breath cycling occurs before the termination of patient effort and the persistent effort triggers a second breath ("double breath"). The phenomenon of "reverse triggering" or "entrainment," can also result in a double breath. This occurs during a machine-triggered breath when the delivered gas flow elicits an effort. Sometimes this simply extends the breath, but, if the effort persists beyond machine breath termination, then a second breath can be triggered. Optimal management of reverse triggering is not clear. Because it often occurs in the setting of high set ventilator rates and sedation, reductions in either of these may be helpful.

*Ventilator-Delivered Flow Pattern.* During an interactive breath, inspiratory muscles are contracting and the ventilator flow delivery should be adequate to provide proper muscle unloading. This does not mean eliminating muscle loads. Instead, it means providing a muscle-loading pattern that resembles normal, comfortable breathing ("synchronous" flow delivery).

In general, flow synchrony is best assessed by clinical assessment and by analyzing the graphic representation of circuit pressure over time. Clinical signs of flow synchrony are a relaxed patient who seems to be flow satisfied. In contrast, flow asynchrony is often manifested as tachypnea, air hunger (dyspnea), and the appearance of "flow starvation." With synchronous flow delivery, the circuit pressure graph should maintain either a steady baseline profile (a continuos positive airway pressure (CPAP) breath) or a convex upward shape (assisted and/or supported breath), which indicates that flow is proportional to demand. Flow asynchrony (and imposed loading) is said to exist when the circuit pressure graph is literally "sucked downward" by effort in excess of flow delivery, often below the baseline. Managing flow asynchrony generally involves either adjustments in the set flow magnitude and/or pattern or converting to a pressure targeted mode with variable flow features.[27,28]

*Breath Cycling.* Cycling asynchrony can occur in one of two ways. First, if the breath lasts beyond the duration of patient effort, an inadequate expiratory time may develop (along with air trapping) and/or patient expiratory efforts may be required to terminate the breath. This can be a particular concern when using pressure support (PS) breaths in OAD: the relatively steady inspiratory flow with PS in these patients coupled with the PS breath termination algorithm may delay breath termination under these conditions. Second, if the breath terminates before the patient effort is finished, then the patient may be left demanding additional flow without any being delivered. Imposed loading and, as noted above, double-breath triggering may result. Management of cycle asynchronies involve adjustments of inspiratory time duration (set inspiratory time, flow-volume combinations, or PS breath termination criteria).[27]

## SILI

PMV breaths can either be controlled (ventilator initiates breath, controls flow delivery, and controls breath cycling duration) or assisted (patients can initiate breaths and often can affect flow delivery and cycling). It is important to realize that, when patients have some control over ultimate breathing frequency and $V_T$, they also have some control over the ultimate end-inspiratory transpulmonary pressure and lung distention. Excessive tidal and end-inspiratory lung distention are well known determinants of VILI.[1–4] There is thus the potential for SILI, despite seemingly "safe" ventilator settings.[10,11]

***Figure 5.*** *Airway pressure, flow, and volume tracings over time in a 70 kg (IBW) patient on 5 cm $H_2O$ pressure support. The patient is at risk for SILI due to the very high tidal volume (910 mL/70 kg = 13 mL/kg IBW) generated by a vigorous inspiratory pressure despite only minimal ventilator pressure. IBW = ideal body weight; SILI = self-inflicted lung injury.*

The classic clinical scenario for this is a patient on low-level PS who still requires CPAP/PEEP and/or backup breathing rates for unreliable drive and/or the need for an endotracheal tube for airway protection. The patient is generating vigorous efforts and the resulting $V_T$ exceeds 10 mL/kg IBW (Fig. 5).

When faced with this situation, the first things a clinician should consider are "fixable" strategies. Are there modifiable causes for excessive drive that can be addressed? Metabolic acidosis? Pain and/or agitation? Poor ventilator settings (rise time, cycle criteria, trigger sensitivity)? Indeed, is there a need for continued endotracheal intubation? An endotracheal tube in the trachea is notoriously uncomfortable. Maybe an extubation trial or a tracheostomy is indicated.

Simple trial-and-error ventilator adjustments are then the next step, Maybe a little additional PS to unload muscles may help. Reduced loading may translate into more properly loaded muscles, which may reduce excessive respiratory drive. In contrast, maybe a little less PS may be more comfortable. Similarly, small adjustments in PEEP or $FiO_2$ could be tried.

When all of these strategies have been exhausted, the clinical conundrum becomes whether to suppress respiratory drive (sedation, neuromuscular blocker [NMB]) or "let it ride." Sedation and/or NMB can certainly reduce and/or eliminate drive but it comes with a cost: delayed extubation and delirium. However, letting a large $V_T$ breathing pattern continue theoretically raises the risk of VILI.

At this point, a reasonable approach might be to further evaluate the risk associated with large $V_T$ breathing. After all, there are many examples of large $V_T$ breathing in healthy individuals: dwellers at high altitude as well as patients with lifelong spinal cord injury. Human lungs seem capable of stretch adaptation over time. Thus, a more careful assessment of lung injury risk is in order.[29–32]

One assessment that has considerable appeal is DP: the pressure required for a $V_T$ to distend alveoli (DP = Pplat – PEEP), described above. DP measurements are not restricted to controlled modes of ventilation and can be determined during any mode of ventilation as long as the patient relaxes briefly during the inspiratory pause. In a patient on standalone PS ventilation, Pplat can also be estimated from a volume-controlled breath with a similar $V_T$ to the $V_T$ during the pressure-supported breath. Because DP reflects compliance characteristics of the respiratory system during $V_T$ delivery, a high DP (>13–19 cm $H_2O$), especially in the setting of regional lung consolidation, might suggest a high risk for SILI. Taken together with other risk factors for VILI (tachypnea, dense consolidation), clinical judgment can be used to determine risk-benefit to sedation versus large $V_T$ tolerance. A low DP, fleeting infiltrates, and respiratory rate (RR) < 15 might justify large volume tolerance; a high DP, extensive infiltrates, and RR > 20 might suggest benefit to sedation or NMB. It is important to note that the above discussion is largely opinion based because meaningful outcome studies on SILI risk management do not exist.

## CONCLUSION

PMV has been used for almost a century around the world to provide safe and effective life support for patients with respiratory failure. Although effective support is readily assessed from gas exchange

measurements, assessments of safe support are more challenging and evidence-based management strategies to provide safe support are constantly evolving. Large randomized controlled studies with meaningful outcome parameters have provided important guidelines over the past 3 decades but clearly more are needed. In going forward, the role of artificial intelligence will likely grow in importance. Artificial intelligence offers the opportunity for analyzing large data bases (both existing and future) to identify best practices in both identifying and managing the challenges described above.

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